IDPH
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NEWBORN SCREENING
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Krabbe Disease

Information for Physicians and Other Health Care Professionals

Definition

Krabbe disease is an inherited metabolic disorder in which harmful amounts of sphingolipids accumulate within lysosomes of cells. Individuals with Krabbe disease do not produce enough of one of the enzymes (galactocerebrosidase or GALC) needed to metabolize lipids. Over time, there is permanent cellular and tissue damage, particularly in the central and peripheral nervous system. Krabbe is classified both as a leukodystrophy and as a lysosomal storage disorder.

Clinical Symptoms

Infantile Krabbe disease is the result of a severe deficiency of GALC. Symptoms begin in the first months of life, with irritability and increased sensitivity to stimuli. Severe mental and motor deterioration ensues with symptoms including seizures, deafness, blindness, paralysis, difficulty swallowing, muscle weakness, and cachexia. In untreated infants, the disease is often fatal before the age of 2 years.

Juvenile or adult Krabbe disease is the result of a less severe deficiency of GALC. Individuals with this later onset form of the disease typically develop symptoms later and live significantly longer than individuals diagnosed with infantile Krabbe disease; however, common late-onset symptoms include psychomotor retardation, blindness and dementia.

Newborn Screening and Definitive Diagnosis

In Illinois, newborn screening for Krabbe disease is performed by determination of the activity of GALC. **If newborn screening results indicate abnormal activity of GALC, referral should be made immediately to a metabolic disease specialist.**

Treatment

Individuals with Krabbe disease are best treated by a team of specialists knowledgeable about the disease, who can offer supportive and symptomatic care. Some individuals with Krabbe disease may benefit from stem cell transplantation which must be performed before the onset of clinical symptoms, typically by one month of age.

Incidence

The precise incidence of Krabbe disease and the percent of cases that represent the infantile form is unclear. It is a rare disorder.

Inheritance Patterns

Krabbe disease is inherited in an autosomal recessive pattern. Parents of a child with Krabbe disease are unaffected, healthy carriers of the condition, and have one normal gene and one abnormal gene. With each pregnancy, carrier parents have a 25 percent chance of having a child with Krabbe disease (inheriting two copies of the abnormal gene). Carrier parents have a 50 percent chance of having a child who is an unaffected carrier, and a 25 percent chance of having an unaffected, non-carrier child. These risks would hold true for each pregnancy. **Genetic counseling is recommended for families planning future pregnancies.**

Pathophysiology
The pathophysiology of Krabbe disease is unclear. There is lysosomal storage of specific sphingolipids but there is also a prominent inflammatory reaction in the brain. There is a progressive leukodystrophy resulting in loss of myelin in the brain and peripheral nerves and progressive neurodegeneration.

Key Points for Parents
It is important to recognize that not all infants identified by newborn screening as having low GALC activity will turn out to have Krabbe disease. However, it is essential that evaluation of such an infant proceed very rapidly so that affected infants can have access to stem cell transplantation if this is the choice of the parents. Make certain that the parents understand the importance of following the pediatrician's and/or specialist's recommendations for additional testing and referrals.

Following Confirmation of Diagnosis
These guidelines should be followed after a diagnosis of Krabbe disease has been confirmed:

1) Follow up with the child's metabolic disease specialist. The specialist should have a relationship with a pediatric stem cell transplantation team.
2) Use a multidisciplinary approach for long-term management including specialists from pediatrics, genetics, and neurology and stem cell transplantation, if appropriate.
3) Ensure that parents understand that treatment for Krabbe disease is not curative and that morbidity cannot always be prevented.
4) Recommend genetic counseling services to help the parents understand the complexity surrounding the carrier state and inheritance of this disease.
5) Provide parents information on support services, such as Hunter's Hope Foundation, United Leukodystrophy Foundation, early intervention service providers, and the local health department.
6) Additional information about newborn screening can be found at:
    - Baby's First Test: http://www.babysfirsttest.org/
      Health Resource and Service Administration (HRSA), Grant no. U36MC16509, Quality Assessment of the Newborn Screening System.
    - National Center for Biotechnology Information: http://www.ncbi.nlm.nih.gov/gtr/
      National Center for Biotechnology Information, U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda MD, 20894 USA.

Although screening for Krabbe is required by the Newborn Metabolic Screening Act [410 ILCS 240], the testing method for this disorder is still under development.